PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| | Applicant's or agent's file reference JHU2010WO | see Form PCT/ISA/220 as, where applicable, item 5 below. | | | | | | | |
|---|---|--|---|--|--|--|--|--|--|
| | International application No. PCT/US04/22698 | International filing date (day/month/y/ 15 July 2004 (15.07.2004) | | | | | | | |
| | Applicant THE JOHNS HOPKINS UNIVERSITY | | | | | | | | |
| • | This international search report has been prepared by this International Searching Authority and is transmitted to the applican according to Article 18. A copy is being transmitted to the International Bureau. This international search report consists of a total of sheets. It is also accompanied by a copy of each prior art document cited in this report. | | | | | | | | |
| | Basis of the Report With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item. | | | | | | | | |
| | The international to this Authority | | translation of the international application furnished | | | | | | |
| | b. With regard to any nucleotic | le and/or amino acid sequence disclos | ed in the international application, see Box No. I. | | | | | | |
| | | unsearchable (See Box No. II) | | | | | | | |
| | 3. Unity of invention is lackin4. With regard to the title, | g (See Box No. III) | | | | | | | |
| | the text is approved as subm | tted by the applicant. | | | | | | | |
|) | i | by this Authority to read as follows: | · | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |
| | With regard to the abstract, | | | | | | | | |
| | the text is approved as submi | tted by the applicant. | | | | | | | |
| | the text has been established, | according to Rule 38.2(b), by this Auti | hority as it appears in Box No. IV. The applicant search report, submit comments to this Authority. | | | | | | |
| | 6. With regard to the drawings, a. the figure of the drawings to be p | ublished with the abstract is Figure No. | · | | | | | | |
| | as suggested by the | applicant. | | | | | | | |
| | as selected by this A | uthority, because the applicant failed to | suggest a figure. | | | | | | |
| | | uthority, because this figure better char | acterizes the invention. | | | | | | |
| | b. none of the figures is to be p | | | | | | | | |
| 1 | Form PCT/ISA/210 (first sheet) (January 200 | 4) | | | | | | | |

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| | Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet) | | | |
|---|--|----------------------|--|--|
| | This | s internati | onal search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: | |
| | 1. | | Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: | |
|) | 2. | | Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically: | |
| | 3. | | Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). | |
| | Box | No. III | Observations where unity of invention is lacking (Continuation of item 3 of first sheet) | |
| | This Plea | Internationse See Co | onal Searching Authority found multiple inventions in this international application, as follows: | |
| | 1. 2. 3. | | As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: | |
| | 4. Rema | ark on Pr | The additional scale frees were accompanied by the applicant's protest. | |
| Ī | | OTAC | No protest accompanied the payment of additional search fees. | |

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International application No.

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| IPC(7) | SIFICATION OF SUBJECT MATTER : A61K 38/00 | | | | | | | | | |
| US CL | : 514/12 | ional alassification | - J IDO | | | | | | | |
| According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED | | | | | | | | | | |
| | | | - | | | | | | | |
| Minimum documentation searched (classification system followed by classification symbols) U.S.: 514/12 | | | | | | | | | | |
| Documentation searched other than minimum documentation to the extent that such documents are included in the fields sea | | | | | | | | | | |
| Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet | | | | | | | | | | |
| | JMENTS CONSIDERED TO BE RELEVANT | | | | | | | | | |
| Category * | Citation of document, with indication, where a | | | Relevant to claim No. | | | | | | |
| Α . | A BERMAN, D. M. et al, Widespread requirement for of digestive tract tumours. Nature. 23 October 2003, | | | | | | | | | |
| A | THAYER, S. P. et al. Hedgehog is an early and late r tumorigenesis. Nature 23 October 2003. Vol. 425, No. | | 1-7 and 12-18 | | | | | | | |
| | | | | | | | | | | |
| Further | documents are listed in the continuation of Box C. | | t family annex. | | | | | | | |
| "A" document | pecial categories of cited documents: defining the general state of the art which is not considered to be of relevance | date and no principle or | et in conflict with the applic theory underlying the inve | | | | | | | |
| | plication or patent published on or after the international filing date | considered | | laimed invention cannot be ed to involve an inventive step | | | | | | |
| | which may throw doubts on priority claim(s) or which is cited to the publication date of another citation or other special reason (as | "Y" document o | of particular relevance; the c to involve an inventive step | laimed invention cannot be when the document is documents, such combination | | | | | | |
| | referring to an oral disclosure, use, exhibition or other means | being obvio | ous to a person skilled in the | art | | | | | | |
| priority da | published prior to the international filing date but later than the attended the control of the | | nember of the same patent i | | | | | | | |
| Date of the actual completion of the international search 16 May 2005 (16.05.2005) | | Date of mailing of the international search report 2 4 MAY 2005 | | | | | | | | |
| | iling address of the ISA/US | Authorized officer January Sheela J. Huff | | | | | | | | |
| Mai Con | I Stop PCT, Attn: ISA/US nmissioner for Patents | | | | | | | | | |
| P.O Alex | . Box 1450 kandria, Virginia 22313-1450 . (703) 305-3230 | Telephone No. 571 | 272-1600 | | | | | | | |
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BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-22, drawn to method of reducing or inhibiting proliferation of cells of a digestive tract tumor using an antagonist wherein said antagonist is a peptide.

Group II, claim(s) 1-22, drawn to method of reducing or inhibiting proliferation of cells of a digestive tract tumor using an antagonist wherein said antagonist is a polynucleotide.

Group III, claim(s) 1-22, drawn to method of reducing or inhibiting proliferation of cells of a digestive tract tumor using an antagonist wherein said antagonist is a peptidomimetic.

Group IV, claim(s) 1-22, drawn to method of reducing or inhibiting proliferation of cells of a digestive tract tumor using an antagonist wherein said antagonist is a small organic molecule.

Group V, claim(s) 1-22, drawn to method of reducing or inhibiting proliferation of cells of a digestive tract tumor using an antagonist wherein said antagonist is an antibody.

Group VI, claim(s) 23-46, drawn to identifying a digestive tract tumor wherein said identification is done using a polypeptide.

Group VII, claim(s) 23-46, drawn to identifying a digestive tract tumor wherein said identification is done using a polynucleotide.

Group VIII, claim(s) 47-67, drawn to identifying an agent to treat digestive tract tumor.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Each of the methods uses a structrually and functionally different product.

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| Continuation of B. FIELDS SEARCHED Item 3: WEST, STN(file biosis): search terms: digestive or esophagus or stomach or pancreas or biliary, hedgehog, tumout or tumor or cancer or malignant | | | | | | | | |
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